

STATEMENT OF WORK

Evaluate/Consolidate Pesticide Exposure Assessments

I. BACKGROUND

Pesticides are chemicals that are deliberately introduced into the environment for a specific purpose. As specified by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA) as amended by the Food Quality Protection Act (FQPA) and is modified by the Pesticide Registration Improvement Act (PRIA), a pesticide may be registered if its use will not result in unreasonable risks or unreasonable adverse effects to humans or the environment. The "risks" in this case are a combination of the inherent toxicity of the pesticide and the extent to which people are exposed to it. The goal of exposure assessments is to present an accurate and realistic picture of human contact with the pesticide on which to base the risk assessment. Companies registering or reregistering pesticides (registrants) submit studies to the Environmental Protection Agency (EPA) that characterize and quantify human exposures resulting from prescribed use of a given pesticide formulation. These pesticide exposure studies, which may focus on either occupational (e.g., mixer/loader/applicator or post-application/reentry) or on residential exposures, are used by EPA for calculation of total body exposure for a given pesticide-use scenario. Before using the data for regulatory purposes, EPA must evaluate the studies to determine their adequacy and to guarantee that appropriate quality assurance (QA) procedures were carried out during the field sampling and laboratory analysis.

The purpose of this requirement is to provide exposure assessments and relevant information necessary for EPA to fulfill the requirements of PRIA, FIFRA, FQPA, FFDCA the Pollution Prevention Act, and any other Executive Order or legislative requirement. The specific objectives are to: (1) perform technical reviews of pesticide human exposure studies and studies related to them, e.g., field residue studies; (2) provide technical support for registration and reregistration actions relating to occupational and residential exposure and risk assessments; (3) provide technical support in developing or revising Standard Operating Procedures (SOPs) and Pesticide Assessment Guidelines for exposure studies; (4) evaluate worker protection issues relating to pesticide exposure and pesticide product labeling; and (5) provide other related technical support in the general subject areas of exposure and risk assessment and pesticides to the Health Effects Division of EPA's Office of Pesticide Programs.

II. Performance Based Contracting Requirements

The Contractor shall perform work on a work assignment basis.

Task 1 Review of Exposure Studies

The Contractor shall perform technical reviews of studies containing pesticide exposure and related data in support of registration, reregistration, and special review activities of HED. These studies may include (1) occupational or residential reentry or post application exposure studies, (2) occupational or residential exposure monitoring data on the subject chemical submitted by registrants on pesticide handling/application operations, (3) exposure related field studies on air, soil, plant, crop, and other residues as needed, (4) physical, chemical properties of a pesticide formulation, active ingredient, or inert relevant to exposure, (5) usage information and data pertaining to potential exposure, (6) exposure studies from the open scientific literature, and (7) exposure studies using data from surrogate pesticide chemicals (e.g., Pesticide Handlers Exposure Database). Reviews of studies on surrogate chemicals may be appropriate when the formulation type, application method, and use pattern are sufficiently similar to those of the chemical under review. In reviewing the assigned studies, the Contractor shall conduct a comprehensive quality assurance and quality control (QA/QC) review.

For each assigned study, a draft written report shall be submitted by the Contractor to the EPA Work Assignment Manager. Draft reports shall (1) document the contents of the studies; (2) note any discrepancies, inadequacies, and unresolved issues; (3) provide appropriate exposure calculations, correlations, and plots; and (4) provide a summary discussion and conclusions resulting from the review.

The Contractor shall prepare the Data Evaluation Review (DER) for Residue Chemistry OPPTS 860 Series Guideline Studies. The Contractor shall also prepare the Summary Document, Chemistry Chapter (RED/TRED), Chemistry Chapter (new chemical, new use and low risk) and Product Chemistry document for OPPTS 830 Series Guideline Studies. Guidance for the preparation of these documents can be found in <http://www.epa.gov/opptsfrs/home/guidelin.htm>.

Task 2 Technical Support for Registration and Reregistration Actions

The Contractor shall provide technical support in developing or revising occupational and residential exposure and risk assessments for registration (new chemicals, new uses, etc.) and reregistration (REDs, TREDs, Low Risk Chemicals) actions, as directed by the EPA Work Assignment Manager. This support may include (1) identification and assessment of occupational handler and post-application exposure scenarios; (2) identification and assessment of residential handler and post-application exposure scenarios; (3) chemistry assessments to support dietary exposure and risk concerns, e.g., the low risk chemicals; (4) identification of risk mitigation measures and the assessment of the mitigation on the resulting risks; (5) aggregate exposure and risk assessments for a single pesticide formulated product, active ingredient or inert; (6) cumulative exposure and risk assessments for a group of chemicals sharing a common mechanism of toxicity; and (7) traditional and probabilistic exposure and risk assessments as

required.

For each assigned task, a draft written report shall be submitted by the Contractor to the EPA Work Assignment Manager. Draft reports shall (1) document the analysis conducted; (2) note any discrepancies, inadequacies, and unresolved issues; (3) provide appropriate exposure calculations, correlations, and plots; and (4) provide a summary discussion and conclusions.

Task 3 Perform Pesticide Exposure and Risk Assessments

The contractor shall perform pesticide exposure and risk assessments in support of registration and reregistration activities. Estimation of potential human health concerns, as a function of toxicity and exposure, is performed using a four-step process: 1) Hazard Identification, 2) Dose-Response Assessment, 3) Exposure Assessment, and 4) Risk Characterization. The Agency will provide the contractor appropriate guidance and computer software to perform single pathway risk assessments, as well as aggregate (multiple pathways, single chemical) and cumulative (multiple chemicals with common mode of toxicity) pathway risk assessments. The exposure duration for these assessments may reflect: one day or less, days or months, years, and or a lifetime. Examples of the types of pesticide risk assessments that could be performed under this contract, include:

- 1 Single pathway, deterministic and probabilistic assessments:
 - 1.1 Food - oral route
 - 1.2 Drinking water -oral route
 - 1.3 Residential - incidental oral, dermal and inhalation route
 - 1.4 Occupational - dermal and inhalation
- 2 Aggregate assessments (single chemical, multiple pathways)
 - 2.1 Dietary (food and water) - oral route
 - 2.2 Dietary and Residential - oral, incidental oral, dermal, inhalation
 - 2.3 Dietary and Occupational - oral, dermal, inhalation
- 3 Cumulative assessment (multiple chemicals common mode of action, multiple pathways)
 - 3.1 Dietary (food and water) - oral route
 - 3.2 Dietary and Residential - oral, incidental oral, dermal, inhalation
 - 3.3 Dietary and Occupational - oral, dermal, inhalation

The format for a cumulative risk assessment is provided in Attachment A. An example of a cumulative risk assessment can be found at <http://www.epa.gov/pesticides/cumulative/rra-op/>.

Performance Standard/Delivery for Task 1 - 3

The contractor is required to summarize data from studies it evaluates and create technical reviews and DERs. These documents shall be prepared as reports that conform to the special formats provided and modification to those formats are authorized by the Project Officer in the

course of the contract. The contractor should use the proposed QC plan to assure accuracy of data extraction from the study or document(s) from which the contractor is evaluating, assuring the absence of mistakes, interpolations, or omissions of data. Due dates for the reports and estimated technical report hours will be specified in the requirements of the work assignment/task order. The contractor shall be required to negotiate unreasonable due dates and technical report hours upon the initial phase of preparing the report.

Method of Surveillance for Task 1-3

Reports prepared by the contractor undergo a secondary review process in OPP. Each report has a designated EPA reviewer who may be either the COR/Work Assignment Manager (WAM) or a staff scientist who is most familiar with the pesticide. The Reviewer conducts a detailed review of the contractor's summary of relevant data and examines the conclusions drawn by the contractor in accordance with the criteria described below. Once the reviewer has finalized the data evaluation in the form of an Agency review, the report may be used in presentations to OPP Science Advisory Councils, (SACs), Science Assessment Review Committees (SARCs), etc. The Reviewer or COR will complete delivery acceptance summary form that notes major discrepancies, omissions, inaccuracies and/or inappropriate data evaluation by contract. The project manager will calculate, quarterly, the average major discrepancies, omissions, inaccuracies and/or inappropriate data evaluation. The COR/ project manager will compare Agency due dates or approved revised due dates to completed date of reports, quarterly and calculate the percentage of late reports. The project manager will compare approved technical review hours with the total technical review hours charged for each task by the contractor, quarterly and calculate the percentage of technical review hours over the Agency approved amount.

Acceptable Quality Limit for Task 1-3

No more than an average error of 5% per quarter is considered acceptable. These errors include some discrepancies, omissions, inaccuracies and/or inappropriate data evaluation is acceptable per quarter. Ninety five percent of the reports per quarter are to be accurately completed within the Agency approved time frame. Ninety nine percent of the technical review hours charged by contractor per quarter are to be in accordance to the Agency approved technical review hours per task.

Disincentive for Task 1-3

A 2% reduction of the fee per quarter if more than 5% major discrepancies, omissions, etc. A 1% reduction per quarter if more than 5% of the reports per quarter are not completed with the Agency approved time frame. A 3% reduction if more than 1% of the technical review hours per quarter exceed the approved amount.

Task 4 Technical Support for Guideline and Standard Operating Procedure Development

The Contractor shall provide technical support in developing or revising Standard Operating Procedures (SOPs), such as the *Standard Operating Procedures (SOPs)* for

Residential Exposure Assessments, as directed by the EPA Work Assignment Manager. Additionally, the Contractor shall provide technical assistance to HED in the revision of Series 875 Pesticide Assessment Guidelines.

Task 5 Worker Protection Evaluations

The Contractor shall assist HED in a number of related worker protection tasks. These tasks may include (1) evaluation, revision, and review of existing worker protection regulations by the Contractor and/or its consultants, (2) participation in field trips to observe the use of various types of protective equipment intended to mitigate exposure during pesticide mixing, loading, and application, or to observe reentry exposure in treated fields, and (3) any other activities that would enhance and support EPA's goal of improving worker protection and safety from pesticide exposures.

Task 6 Workshops, Seminars, and Training

The Contractor shall identify recognized experts in the area of postapplication and reentry exposures and related field exposures. When needed, the Contractor shall convene a roundtable meeting with such experts to resolve generic issues regarding reentry exposure quantization methodologies and related issues. Additionally, the contractor shall conduct literature searches and prepare technical publications such as workshop summaries, minutes following seminars and other meetings, and journal articles.

Method of Surveillance for Task 4, 5 & 6

The COR or Reviewer shall compare contractor revised guidelines, SOPs, or regulations with current procedures per a review board and analyze the new guidelines, SOPs, or regulations for errors of problematic procedures.

The CORs or Reviewers shall attend and observe all Agency driven workshops, seminars, and training for consistency and relevancy to Agency.

Acceptable Quality Limit for Task 4, 5, & 6

Revisions shall address the categories of data required, the methods by which that data should be obtained, methods for evaluating such data, submission of protocols, international harmonization (e.g., OECD, NAFTA), and development of exposure assessment criteria. In reviewing these Guideline documents, the Contractor's efforts shall identify and evaluate other Agency guidance on exposure assessment and exposure parameter values, such as those noted in the Exposure Factors Handbook (EPA/600/P-95/002Fa-c).

The Contractor shall also provide technical support to EPA in developing testing requirements for CFR 40, Part 158, if requested. If requested, the Contractor shall (1) submit the proposed revisions of Series 875 Guidelines to peer reviewers approved by the EPA Work Assignment Manager; (2) submit a synopsis of the peer review comments; and (3) provide technical recommendations thereon. All contractor deliverables shall result in improving the

worker protection and safety from pesticide exposure.

Disincentive for Task 4, 5, & 6

EPA may terminate the contract for default if annual reports show that revised guidelines, SOPs, regulation, workshops, seminars or training composed or derived by the contractor contain faulty information which results in harming humans exposed to pesticides.

Task 7 Technical Support for Exposure Model and Database Development and Enhancement

The Contractor shall develop, expand, modify databases and models used by OPP for exposure and risk assessments. For example, if so directed, the Contractor shall review additional studies for inclusion in the Pesticide Handler Exposure Database (PHED). Related activities may include reviewing hard copy studies and electronic data, contacting the data generator to obtain missing information, entering the data into PHED, and conducting quality assurance testing of the data once entered into PHED. The Contractor shall also provide other related technical support, such as the incorporation of revisions into the PHED software in response to user comments and conducting user training. In addition, the contractor shall develop models to support exposure and risk assessments for pesticide products, including inert ingredients, e.g., the Pesticide Inert Risk Assessment Tool (PIRAT).

Method of Surveillance for Task 7

The COR or Reviewer shall evaluate the database to determine if any inaccuracies exist such as erroneous data, insufficient data, etc. The COR or Reviewer will report to contractor all found problems promptly. The COR or Review will semi-annually summarize repetitive errors or inaccuracies.

Acceptable Quality Limit for Task 7

A 100% of all requested database supported task orders/work assignments completed accurately within the time frame specified. Address all requests within a 24 hour period.

Disincentive for Task 7

A 1% reduction semi-annually if repeated errors exist after resolution has been ordered. A 1% reduction if the contractor does not respond to task orders/work assignments within a 24 hour period and/or a 1% reduction semi-annually if the reports are not completed with the Agency approved.

Task 8 Quick Response and Agency Interface Activities

The Contractor shall provide quick turn-around technical support relating to occupational and residential exposure and risk assessments as requested by the EPA Work Assignment Manager. Additionally, the Contractor shall also assist HED in interfacing with other

Government agency requests, to the extent that such requests are feasible and relate to the general scope of this Statement of Work.

Method of Surveillance for Task 8

The COR shall compare and record Agency agreed upon to due dates to actual completed dates of task, monthly, to determine if any slippage has repeatedly occurred. A report will be created quarterly to calculate the percentage of late reports. COR shall note whether more than 90% of the approved direct labor hours were used before a request for more hours was requested. Also, the COR shall monitor the Contractors' request for additional time or hours to complete task. The COR or Reviewer will report to contractor all found problems promptly. The COR or Reviewer will semi-annually summarize repetitive errors or inaccuracies.

Acceptable Quality Limit for Task 8

The Contractor shall complete all task on time 99% of the time. The contractor shall not charge more direct labor hours than the agency agreed to complete a task. The Contractor shall not be inconsistent in time needed to complete task of similar nature. The contractor shall request for additional direct hours per task before 60% of the approved task order direct labor hours are used. All problems found by Contractor when completing task should be addressed to Agency for resolution when found.

Disincentive for Task 8

A 1% reduction in fee, semi-annually, shall be warranted if task are not completed on time 99% of the time. Agency shall not pay for unauthorized charges such as unapproved direct labor hours, training and travel. A 1% reduction in fee shall be order, semi-annually, if repeated errors exist after resolution has be ordered. Agency may not reimburse contractor for additional direct labor hours requested to complete a task if request for additional hours are requested after completion of task.

All deliverables shall be in compliance with the Section 508 Accessibility Standards of the Rehabilitation Act, of 1973 and Amendments of 1998. When preparing deliverables, the contractor shall refer to the most recent version of the 508 Standards, which can be found at: <http://www.access-board.gov/sec508/guide/>

**HED RISK ASSESSMENT DOCUMENT (RAD)
FORMAT AND RISK CHARACTERIZATION GUIDANCE**

Replaces HED SOP 2000.2

Draft: 1-June-2004

The purpose of HED SOP 2004.01 is to provide guidance to HED Risk Assessment Teams on developing and completing a final Human Health Risk Assessment Document in HED's new risk assessment process. This document provides the following:

- 1) A generic risk assessment outline for Registration Eligibility Documents (REDs), Tolerance Reassessment Eligibility Documents (TREDs), New Active Ingredients, and Section 3 Registrations for New Uses of Old Chemicals. The generic outline is a "backbone" document in which the codes for generation of the Table of Contents are already embedded. The generic outline is intended to be modified as needed to accommodate the needs of the type assessment being conducted.
- 2) Reviewer guidance for elements to consider in the assessment and characterization of the risk conclusions. Under each of the elements presented, questions/comments are provided to help direct the RA Team. These questions are not meant to be all encompassing, nor does every question apply to all scenarios or risk assessments, they are provided as a guide. The RA Team should consider the unique aspects of the risk assessment in considering the questions posed below, and may want to expand into other areas for more complex or unique situations.
- 3) Standard Table Formats

The RAD initiates as a draft document for RARC 1. The draft document presented to RARC 1 contains at a minimum Section 0.0 (Proposed Review and Risk Assessment Strategy). However, RA-Teams are advised to complete as much of the full RAD outline as possible with particular focus on completion of the template tables. While the completeness of the data review will be a factor in determining the extent to which the outline and tables can be completed, RA-Teams are encouraged to utilize the template tables as much as possible for presentation of probable risk levels. As recommended by RARC 1, the Draft RAD may continue on to HEXARC and/or RARC 2. Section 0.0 is presented in preliminary documents only and is removed from the final risk assessment document in the final Branch QA/QC process.

0.0 PROPOSED REVIEW AND RISK ASSESSMENT STRATEGY

The following guidance is intended to assist RA Teams in preparation of their proposed review and risk assessment strategy. In addition to the guidance here, RA Teams are encouraged to utilize more in-depth guidance and resource pointers provided in the full RAD outline.

0.1 Purpose of Risk Assessment

Describe why the risk assessment is being conducted and estimate the target completion date based on the PRIA decision time frame or reregistration schedule.

0.2 Exposure Profile

Briefly describe the existing/proposed use patterns (use summary tables).

What exposure pathways (e.g., food, water, non-occupational [residential], occupational) will result from the use of this chemical?

What is the likelihood of quantifiable residues in food? What data sources are available to estimate residues in food (residue field trials, USDA PDP, market basket survey, etc)? Are residues mostly on plant surfaces or are they systemic? Is there likelihood of transfer of residues to meat and/or milk? What is the general metabolic profile in plants and livestock? Are the terminal residues predominately parent or are metabolites in greater abundance than the parent compound? Are the metabolic pathways for plants and livestock similar?

Is this compound or any of its environmental degradates likely to be present in water? Is the compound or any of its environmental degradates mobile and/or persistent? Can water monitoring data be used quantitatively in the risk assessment?

What non-occupational (residential) populations will likely be exposed and how (e.g., residential adult handler, residential post application adult and/or child)? What are the expected non-dietary exposure routes (e.g., dermal, inhalation, incidental oral)? What are the expected non-dietary exposure durations (e.g., short-, intermediate-, long-term)?

What are the likely exposures for occupational handlers and post application workers?

Is this chemical or its metabolites/degradates associated with chemicals being monitored by NHANES (total population) or the Agricultural Health Study (pesticide handlers and family members)?

0.3 Review Status

What level of information is currently available for hazard identification and exposure assessment (including receipt of additional or new data)? Have data been required to meet conditions of registration? Is there an existing HIARC document? Are there new data that would alter past HIARC decisions? Are the past HIARC decisions in accordance with current policies? Is there an existing MARC document? Will it be necessary to establish or reaffirm decisions on residues for tolerance expression and risk assessment?

0.4 Initial Endpoint, Uncertainty Factor, and FQPA Selection

What are the effects of this chemical? Is this chemical a potential or known carcinogen; a developmental/reproductive toxicant; an endocrine disruptor; a neurotoxicant? What is the overall toxicity profile? Provide a toxicity profile table (e.g., Table 4.2). Are adequate hazard studies (including those from the published literature) available for evaluation of risk to infants and children? Do these studies show increased susceptibility to infants and children? Is the special FQPA Safety Factor retained to account for any residual uncertainties for pre- and/or postnatal toxicity concerns? Is the special FQPA Safety Factor retained for exposure concerns? Are other uncertainty factors (UFs) needed to derive acute and chronic RfDs or to provide appropriate safety margins for non-dietary exposure? Provide a summary table of doses and endpoints for risk assessment (e.g., Table 4.4) along with rationale for endpoint selection.

0.5 Initial Determination of Metabolites and Degradates for Risk Assessment Tolerance Expression

What metabolites and degradates are likely to be included in the exposure assessment? What metabolites and degradates are likely to be included in the tolerance expression? Provide a summary table (e.g., Table 3.6)

0.6 Hazard and Exposure Database Deficiencies

If a new chemical screen has been conducted, what data deficiencies, if any, were identified? Have data been required to meet conditions of existing registrations? Have confirmatory data been required as part of a RED/TRED? Have additional toxicology study data been required by HIARC or CARC? To what extent will the lack of data impact the ability to complete a risk assessment with reasonable certainty?

0.7 Existing or Estimated Risk

*If the ingredient has existing registrations, to what extent will proposed new uses alter current levels of dietary and non-dietary exposure? To the extent possible, identify probable dietary and non-dietary risk levels.
If the ingredient is a new chemical, identify probable dietary and non-dietary risk*

levels.

0.8 Proposed Review and Assessment Strategy

What is the Team's proposed plan for risk assessment development? Does the Team propose a full assessment path (e.g., HEXARC and RARC2)? What existing documents will the team use to support the final risk assessment? What additional documents will be needed to support the final risk assessment? What is the estimated timeline for completion?



In addition to indicating that the Risk Assessment Document (RAD) is final and ready for distribution, the cover memo serves as a collection of critical information required to properly store the document for future retrieval and reference. Key data are also taken from the cover memo and entered into the OPPIN Risk Assessment Document Database (RADD).

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: [Month/Day/Year]

Enter the date that the cover memo is signed indicating the attached RAD is Final (complete).

MEMORANDUM

SUBJECT: [*ingredient:*] HED Chapter of the Reregistration Eligibility Decision Document (RED). PC Code: xxxxxx, Case #: xxxx, DP Barcode: Dxxxxxx.

The Subject line should contain: the names of all ingredient(s) considered in the risk assessment; the document type; the PC Code(s) of the ingredient(s) included; the assigned petition or case number (depending on the type of regulatory action being addressed); and the assigned DP Barcode(s).

Regulatory Action: [*Phase I Reregistration Action*]
Risk Assessment Type: [*Single Chemical Aggregate*]

In order to file the risk assessment properly in OPPIN RADD, indicate the type of regulatory action addressed in the attached risk assessment and the type of risk assessment conducted.

Regulatory Actions include: Section 3, Section 18, and Section 24(c) registration actions; Reregistration Eligibility Decisions (Phases I-VI); Tolerance Reassessment Progress and Interim Risk Management Decisions; and New Chemicals Screens.

Risk Assessment Types include: Single Chemical/Aggregate; Single Chemical/No Aggregate; Multiple Chemicals/Aggregate; Multiple Chemicals/No Aggregate; and Cumulative.

OR

[*ingredient*.] Human Health Risk Assessment for Proposed Uses on [*crop(s)*]. PC Code: xxxxxx, Petition No: XFXXXX, DP Barcode: Dxxxxxx.

Regulatory Action: [*Section 3 Registration Action*]
Risk Assessment Type: [*Single Chemical Aggregate*]

FROM: Name, Title
Branch
Health Effects Division (7509C)

Enter the name of the risk assessor or the lead for the risk assessment team (point of contact for the attached RAD).

AND

Team Reviewers, Title
Branch
Health Effects Division (7509C)

Enter the name(s) of the risk assessment team members that completed the attached RAD.

THROUGH: Name, Branch Senior Scientist
Branch
Health Effects Division (7509C)

Enter the name of the approving official (typically the Senior Scientist or Branch Chief) for the attached RAD.

TO: PM/CRM
Branch
RD/SRRD (Mail Stop)

Enter the name of the Project Manager (RD) or Chemical Review Manager (SRRD) to receive the attached RAD.

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1.0 Executive Summary

**This is intended to be a non-technical characterization of the risk assessment.
As such, numbers (e.g., NOAELs, exposure estimates, risk estimates) can be kept to a minimum.**

Describe, at an overview level, why the risk assessment was conducted, the chemical(s) addressed, and the use sites. Briefly describe the use patterns, including modes of application and maximum application rates.

Discuss the targeted pests and the mode of action. Characterize how the mode of action relates to human health. Characterize the toxicology database in terms of observed effects and qualitative dose levels that caused those effects. Discuss in a general sense how the toxicological data are used in the risk assessment,

Discuss the adequacy of the residue chemistry data as it relates to assessing human exposure, including any special considerations unique to the chemical.

Discuss the adequacy of the environmental fate data as it relates to assessing human exposure.

Discuss the adequacy of the data available to assess non-occupational, non-dietary (i.e., residential) exposures, including any special considerations unique to the chemical.

Characterize any aggregate exposure scenarios, including the degree of confidence in risk estimates (level of refinement) and general statements about the risk levels. A brief discussion of mitigation measures may be appropriate.

Characterize occupational exposure and risk estimates, including minimal acceptable PPE and any exposure scenarios of particular concern.

Make overall risk conclusions as related to human health, for the action being addressed by the risk assessment. Provide a short discussion of data gaps and/or clarifications as appropriate.

2.0 Ingredient Profile

What is the identity of this compound and to what general class of compounds does it belong (e.g., organophosphate, triazine, etc.)? Is the compound a fungicide, insecticide, herbicide, or other? What target pests does it control and by what mode of action?

How is the compound formulated? What are the proposed or currently registered formulation classes (e.g., wettable powder, emulsifiable concentrate, etc.). What is the range of % active ingredient?

What type of equipment is used for application? What is the timing and frequency of application (e.g., pre-plant, multiple foliar, post harvest)? What are typical PHIs? What are the REIs? What is the range of application rates?

NOTE: Tables 2.1, 2.2 and 2.3 can be taken directly from a Residue Chemistry Chapter/ Summary Document. There may be alternate formats of Table 2.1 that are more appropriate for reregistration chemicals which can be inserted as an Appendix to the RAD at the discretion of the RA Team.

2.1 Summary of Registered/Proposed Uses

Table 2.1. Summary of Directions for Use of [Chemical].						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Use Site 1						
Use Site 2						
Use Site 3						

2.2 Structure and Nomenclature

Are there any isomeric forms of the compound? Are there any impurities of known toxicological concern present in the technical formulation(s) (e.g., nitrosamines, dioxins, PCBs, etc.)?

TABLE 2.2. Test Compound Nomenclature	
Chemical Structure	[Paste Chemical Structure Here.]
Empirical Formula	
Common name	
Company experimental name	
IUPAC name	
CAS name	

CAS Registry Number	
End-use product/EP	
Chemical Class	
Known Impurities of Concern	

2.3 Physical and Chemical Properties

How might the p-chem properties of this ingredient affect exposure and/or disposition of residues in the body. What do the vapor pressure or solubility properties indicate about the behavior of the chemical related to human exposure patterns? Is there an increased likelihood of inhalation or dermal exposure because of the chemical properties of the pesticide?

TABLE 2.3. Physicochemical Properties		
Parameter	Value	Reference
Molecular Weight		
Melting point/range		
pH		
Density		
Water solubility (20 C)		
Solvent solubility (temperature not specified)		
Vapor pressure (25 C)		
Dissociation constant, pKa		
Octanol/water partition coefficient, logP _{ow} (25 C)		
UV/visible absorption spectrum		

3.0 Metabolism Assessment



RESOURCE: “Criteria for Inclusion of Pesticide Metabolites and Degradates in Risk Assessments and Tolerance Expressions” 22-December-2003

NOTE: In the event the RAD goes to HEXARC, there may be additional information that will be required. Refer to Appendix 3.0 for additional guidance.

3.1 Comparative Metabolic Profile

A summary of all rat metabolism studies should be included, specifically highlighting the significant metabolites identified in rat excreta and tissues (if available). The relative amount of each metabolite found should be summarized. Metabolites that are found in plants, water, and/or livestock that are not found in the rat should be highlighted. Also include any available human data. Provide a description of the rat, plant and livestock metabolism pathways and a numerical summary of major rat metabolites and minor metabolites that were also found in the livestock and plant metabolism studies.

3.2 Nature of the Residue in Foods

3.2.1. Description of Primary Crop Metabolism

Description of plant metabolism pathways, including identification of major metabolites and specific routes of biotransformation.

3.2.2 Description of Livestock Metabolism

Description of livestock metabolism pathways, including identification of major metabolites and specific routes of biotransformation.

3.2.3 Description of Rotational Crop Metabolism, including identification of major metabolites and specific routes of biotransformation

Description of residues in rotational crops, including identification of major metabolites (and environmental degradates taken up by the plant) and specific routes of biotransformation.

3.3 Environmental Degradation

Description of the environmental degradation of the pesticide, with an emphasis on how the pesticide and/or its degradates could reach drinking water resources. Quantitative information on the major degradates should be included.

3.4 Tabular Summary of Metabolites and Degradates

Table 3.4 may be included in Appendix 3.0 at the RA Team's discretion.

Table 3.4. Tabular Summary of Metabolites and Degradates				
Chemical Name (other names in parenthesis)	Commodity	Percent TRR (PPM) ¹		Structure
		Matrices - Major Residue (>10%TRR)	Matrices - Minor Residue (<10%TRR)	
Parent	Crop 1			
	Crop 2			
	Crop 3			
	Rotational Crops			
	Ruminant			
	Poultry			
	Rat			
	Water			
Degradate (n)	Crop 1			
	Crop 2			
	Crop 3			
	Rotational Crops			
	Ruminant			
	Poultry			
	Rat			
	Water			
<i>The final row of the table should have a concise summary of relevant parameters.</i> Crop 1; MRID No.; Application Rate; Level of exaggeration compared to label rate; timing; pre-harvest interval. Livestock 1; MRID No.; Feeding Level; Level of exaggeration compared to maximum dietary burden; days of dosing; pre-slaughter interval. Rotational Crops; MRID No.; specific crops, Level of exaggeration compared to label rate; application type; range of plant-back intervals. Rat 1; MRID No.; dosing level; other specific				
<i>Examples:</i> <i>Apple, 12345678; 1 lb ai/A; 3X rate; petal fall; 90.</i> <i>Lettuce, 12345678, 3 lb ai/A; 5x; immature leaves, 10 days.</i> <i>Goats; 12345678; 10 ppm; 25X MTDB; 5 days; 12 hour PSI.</i> <i>Rotational Crops; 12345678; 1x, applied to bare soil;30-120 day PBI</i> <i>Rat Metabolism; 20 mg gavage dose; Sprague-Dawley, 1 day depuration.</i>				

3.5 Toxicity Profile of Major Metabolites and Degradates

A description of the relative toxicity of the major metabolites and degradates. May include a structure-activity relationship profile, a structural comparison to the parent compound (and therefore toxicity comparison), literature information on the degradates, toxicity data on the metabolites/degradates, and any other information that would describe the toxicity of the metabolites and degradates.

3.6 Summary of Residues for Tolerance Expression and Risk Assessment

3.6.1 Tabular Summary

Table 3.6. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression			
Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop		
	Rotational Crop		
Livestock	Ruminant		
	Poultry		
Drinking Water			Not Applicable

3.6.2 Rationale for Inclusion of Metabolites and Degradates

A justification for inclusion of metabolites and degradates should include both exposure and hazard rationale.

4.0 Hazard Characterization/Assessment

NOTE: **Section 4.0** replaces the toxicity chapter and the HIARC document. It contains a hazard characterization narrative (Section 4.1); acute toxicity profile table; toxicity profile of test substance(s); executive summaries of studies used for the FQPA evaluation and endpoint selections (Section 4.2); and the endpoint selection table (Section 4.4). Additional hazard characterization guidance for completion of **Section 4.1** is currently being developed and will be incorporated in the revision of this interim RAD SOP. **Sections 4.2, 4.3, and 4.4** are essentially identical to the format and content of a HIARC Report. Guidance for completion of these sections may be found below:



RESOURCES:

- 1) Guidance for Hazard Identification and Toxicity Endpoint Selection (2-February 2004) [See ▼Guidance (Committee) ➤HIARC]
- 2) Proposed Data Presentation to HIARC (Revised 03/25/03) [See ▼Templates ➤HIARC 2003HIARCPROPOSAL.wpd]

4.1 Hazard Characterization

The hazard characterization narrative is not intended to simply list NOAEL/LOAELs and effects from each study or a shortened version of the executive summaries. Hazard characterization is intended to provide a comprehensive look at the overall toxicity of a chemical. The following questions do not need to each be specifically answered as asked, but they are intended to provide the hazard assessor guidance on the types of questions the hazard characterization should address.

Are the toxic effects typical of this class of compound (e.g., organophosphorous ChE inhibition)? Are the observed effects unique to the chemical class?

What are the toxicologically-significant adverse effects? Do these effects occur among all tests and test species? At what dose levels did these effects occur? Is there a causal (dose-response) relationship between the effects and the doses tested? Are the effects noted in short-term studies similar to those in longer-term studies, do they occur at lower doses in the longer term studies and do they increase in severity with longer exposure? Is the toxic effect and/or target organ the same across species or is it a species-specific phenomenon? Is there a sex-specific effect or sex-related differences in sensitivity?

Are there dermal and inhalation toxicity studies available? Do they show the same or different toxic effects? Do the toxic effects occur at the same or different dose ranges?

Are there route-specific endpoints for all exposure pathways? If not, characterize any route-to-route determinations that were used. Are there adequate dermal absorption or other relevant (e.g., metabolism, pharmacokinetics) data available? If not, what assumptions can be made regarding dermal absorption and what is the rationale?

Does the chemical cause reproductive or developmental toxicity and do the effects occur above, at, or below parentally-toxic doses?

Is there any indication of increased susceptibility of the fetus/pups noted in the developmental toxicity or reproductive toxicity studies (FQPA evaluation)? If so, comment on the severity of the effects in the young as compared to the adult animals. Is there any evidence of neurotoxicity in the database? Are there any critical data gaps (such as those studies critical to the assessment of potential hazard to infants and children?)

Is the chemical positive for mutagenicity? Do in vivo studies support in vitro findings? Does the mutagenicity database support the findings in related studies, if so, what are the implications? Is the chemical considered a carcinogen? If so, what is the classification and basis for the classification? What are the primary tumor sites? What is the methodology recommended for the cancer risk analysis? If an MOE approach is used for cancer, is the MOC for infants/kids the same as the MOC for other subpopulations?

Does the toxicity profile indicate a potential concern for estrogen, androgen and/or thyroid mediated toxicity?

Have significant metabolites of concern been identified? What is known or can be predicted about the toxicity of the metabolites and how does the toxicity compare to the parent (less, the same or greater than the parent)? Are the metabolites to be considered for regulatory and risk assessment purposes?

What is the scientific (and regulatory) quality of the toxicology data base as well as the associated confidence in the hazard and dose-response assessments?

Table 4.1a Acute Toxicity Profile - Test Substance				
Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral [species]	[]	LD ₅₀ = [] mg/kg	[]
870.1200	Acute dermal [species]	[]	LD ₅₀ = [] mg/kg	[]
870.1300	Acute inhalation [species]	[]	LC ₅₀ = [] mg/L	[]
870.2400	Acute eye irritation [species]	[]	[]	[]
870.2500	Acute dermal irritation [species]	[]	[]	[]
870.2600	Skin sensitization [species]	[]	[]	[]

Table 4.1b Subchronic, Chronic and Other Toxicity Profile		
Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 90-Day oral toxicity (species)	43214321 (2004) Acceptable/guideline 0, 200, 800, 400 ppm M: 0, 9, 35, 180 mg/kg/d F: 0, 11, 45, 244 mg/kg/d	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3150 90-Day oral toxicity (species)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3200 21/28-Day dermal toxicity (species)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3250 90-Day dermal toxicity (species)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3465 90-Day inhalation toxicity (species)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3700a Prenatal developmental in (species)	[]	Maternal NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on []. Developmental NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3700b Prenatal developmental in (species)	[]	Maternal NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on []. Developmental NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.3800 Reproduction and	[]	Parental/Systemic NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].

Table 4.1b Subchronic, Chronic and Other Toxicity Profile

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
fertility effects (species)		Reproductive NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on []. Offspring NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.4100a Chronic toxicity (species)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.4100b Chronic toxicity (dog)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.4200 Carcinogenicity (rat)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on []. (no) evidence of carcinogenicity
870.4300 Carcinogenicity (mouse)	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on []. (no) evidence of carcinogenicity
Gene Mutation 870.[] Insert mutation studies here (add lines as needed)	[]	
Cytogenetics 870.[] Insert mutation studies here (add lines as needed)	[]	
Other Effects 870.[] Insert mutation studies here (add lines as needed)	[]	
870.6200a Acute neurotoxicity screening battery	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.6200b Subchronic neurotoxicity screening battery	[]	NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.6300 Developmental neurotoxicity	[]	Maternal NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on []. Offspring NOAEL = [] mg/kg/day LOAEL = [] mg/kg/day based on [].
870.7485 Metabolism and pharmacokinetics	[]	[]

Table 4.1b Subchronic, Chronic and Other Toxicity Profile		
Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
(species)		
870.7600 Dermal penetration (species)	[]	[]
Special studies	[]	[]

4.2 FQPA Hazard Considerations

4.2.1 Adequacy of the Toxicity Data Base

4.2.2 Evidence of Neurotoxicity

4.2.3 Developmental Toxicity Studies

4.2.4 Reproductive Toxicity Study

4.2.5 Additional Information from Literature Sources

4.2.6 Pre-and/or Postnatal Toxicity

4.2.6.1 Determination of Susceptibility

4.2.6.2 Degree of Concern Analysis and Residual Uncertainties for Pre and/or Post-natal Susceptibility

4.3 Recommendation for a Developmental Neurotoxicity Study

4.3.1 Evidence that supports requiring a Developmental Neurotoxicity study

4.3.2 Evidence that supports not requiring for a Developmental Neurotoxicity study

4.3.2.1 Rationale for the UF_{DB} (when a DNT is recommended)

4.4 Hazard Identification and Toxicity Endpoint Selection

4.4.1 Acute Reference Dose (aRfD) - Females age 13-49

4.4.2 Acute Reference Dose (aRfD) - General Population

4.4.3 Chronic Reference Dose (cRfD)

4.4.4 Incidental Oral Exposure (Short and Intermediate Term)

4.4.5 Dermal Absorption

4.4.6 Dermal Exposure (Short, Intermediate and Long Term)

4.4.7 Inhalation Exposure (Short, Intermediate and Long Term)

4.4.8 Margins of Exposure

4.4.9 Recommendation for Aggregate Exposure Risk Assessments

4.4.10 Classification of Carcinogenic Potential

Table 4.4. Summary of Toxicological Doses and Endpoints for Chemical for Use in Human Risk Assessments			
Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (females 13-49)			
Acute Dietary (general population)			
Chronic Dietary (all populations)			
Incidental Oral Short-Term (1 - 30 days)			
Incidental Oral Intermediate-Term (1 - 6 months)			
Dermal Short-Term (1 - 30 days)			
Dermal Intermediate-Term (1 - 6 months)			

Table 4.4. Summary of Toxicological Doses and Endpoints for Chemical for Use in Human Risk Assessments			
Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Long-Term (> 6 months)			
Inhalation Short-Term (1 - 30 days)			
Inhalation Intermediate-Term (1 - 6 months)			
Inhalation Long-Term (> 6 months)			
Cancer (oral, dermal, inhalation)	Classification:		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

* Refer to Section 4.5

4.5 Special FQPA Safety Factor

RESOURCE: 2002 OPP FQPA 10X Guidance; www.epa.gov/pesticides/trac/science/determ.pdf

Record the size of the Special FQPA Safety Factor needed to account for any residual uncertainty resulting from the integration of hazard concerns (from Section 4.2) and exposure concerns (Section 6.0). Describe the rationale for both the size and the need for the factor. Include each applicable risk assessment scenario if the factor differs by duration or population subgroup.

In cases when the Special FQPA Safety Factor is removed, explain why it is not required.

Example Standard Language - FQPA Special SF Removed

Based on the hazard data, the [HIARC/HEXARC/RARC] recommended the special FQPA SF be reduced to 1x because there are no/low concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity. The [chemical] risk assessment team evaluated the quality of the exposure data; and, based on these data, recommended that the special FQPA SF be reduced to 1x. The recommendation is based on the following:

- The dietary food exposure assessment utilizes proposed tolerance level or higher residues and 100% CT information for all commodities. By using these screening-level assessments, chronic exposures/risks will not be underestimated.
- The dietary drinking water assessment (Tier 1 estimates) utilizes values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations.
- The residential exposure assessment utilizes: activity specific transfer coefficients and chemical-specific turf transferable residue (TTR) studies for the post-application scenario. The refined residential assessment is based on reliable data and is unlikely to underestimate exposure/risk.

4.6 Endocrine disruption

The following standard language has been developed with OGC for use in all OPP risk assessment documents. As Agency policies are developed or modified, this language will be updated.

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

[Insert here a statement specific to the assessed chemical, such as:

In the available toxicity studies on [chemical], there was no estrogen, androgen, and/or thyroid mediated toxicity.

Effects were observed in tests which indicated potential estrogen, androgen, and/or thyroid mediated toxicity. Describe those observations that were seen.]

When additional appropriate screening and/or testing protocols being considered under the Agency’s EDSP have been developed, [chemical] may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

5.0 Public Health Data

Please contact Jerry Blondell or Monica Span to obtain an incident report. Please contact Ruth Allen or David Miller to obtain additional information on or evaluation of NHANES or AG HEALTH data

5.1 Incident Reports

5.2 Other

6.0 Exposure Characterization/Assessment

6.1 Dietary Exposure/Risk Pathway

6.1.1 Residue Profile

NOTE: Utilize the Executive Summary from the Chemistry Chapter/Summary Document.

Describe the metabolic pathway in plants and animals. Are the pathways in plants and animals similar? Are the residues to be included in the tolerance expression the same as those included in the risk assessment? If not, what modifying factors were used to adjust residue values. To what extent do the adjustments over or underestimate exposure?

What is the distribution of residues edible portions of plants (which crops or crop parts have the highest residues)? Are residues mostly on surfaces (fruit peels, grain coatings) with no detectable residue in pulp or meats? Were residues consistently below the LOQ or LOD in all crops or in certain crops? If residue levels varied significantly was it a function of use pattern?

What level of confidence in the data being used to determine tolerances? How much data were available (minimum field trials or broad range of trials with multiple use patterns/formulations)? Were residues consistently below the LOQ or LOD in all crops or in certain crops? If residue levels varied significantly was it a function of use pattern?

Is adequate enforcement methodology available to enforce the proposed tolerances? Briefly describe the methodology.

6.1.2 Acute and Chronic Dietary Exposure and Risk

**Reference the Dietary Exposure Memo here.
Include the Tolerance Reassessment Summary and Table in an Appendix.**

Paste the executive summary from the Dietary Exposure Memo here.

NOTE: The Agency is currently utilizing both the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 1.30) and the Lifeline Model Version 2.0 to conduct dietary risk assessments. RA Teams may elect to use one of

the following table formats, depending on whether one or both models were used to assess dietary risk.

Table 6.1 Summary of Dietary Exposure and Risk for [Chemical].								
Population Subgroup^a	Acute Dietary (XXth Percentile)			Chronic Dietary			Cancer Dietary	
	aPAD, mg/kg	Exposure, mg/kg/day^b	% aPAD	cPAD, mg/kg/day	Exposure, mg/kg/day^b	% cPAD	Exposure mg/kg/day	Risk
General U.S. Population								
All Infants (< 1 yr)								
Children 1-2 yrs								
Children 3-5 yrs								
Children 6-12 yrs								
Youth 13-19 yrs								
Adults 20-49 yrs								
Adults 50+ yrs								
Females 13-49 yrs								

^a The values for the population with the highest risk for each type of risk assessment are bolded.

^b Reported to 2 significant figures.

Table 6.1. Result of Acute and Chronic Dietary Exposure and Risk Estimates for [Chemical].					
Population Subgroup	PAD, mg/kg/day	DEEM-FCID		Lifeline	
		Exposure, mg/kg/day	% PAD	Exposure, mg/kg/day	%PAD
Acute Dietary Estimates (99.9 th Percentile of Exposure)					
Include the appropriate populations					
Chronic Dietary Estimates					
U.S. Population					
All infants (< 1 yr)					
Children 1-2 yrs					
Children 3-5 yrs					
Children 6-12 yrs					
Youth 13-19 yrs					
Adults 20-49 yrs					
Adults 50+ yrs					
Females 13-49 yrs					
Cancer Dietary Estimate					
U.S. Population					

6.2 Water Exposure/Risk Pathway

Reference the drinking water memo here (if available).

Describe how the drinking water exposure is being addressed (monitoring vs. modeled values) and characterize the level of refinement for model input parameters and outputs. Address any issues regarding the residues of concern. Characterize the uncertainties associated with the selected EDWC.

Exposure Duration	[Chemical]	
	Surface Water Conc., ppb ^a	Ground Water Conc., ppb ^b
Acute		
Chronic (non-cancer)		
Chronic (cancer)		

^a From the Tier II PRZM-EXAMS - Index Reservoir model. Input parameters are based on ...

^b From the SCI-GROW model assuming a maximum seasonal use rate of XXX lb ai/A, a K_{oc} of XXX, and a half-life of XXXX days.

6.3 Residential (Non-Occupational) Exposure/Risk Pathway

Reference the residential exposure assessment memo here.

Describe any home/recreational use scenarios and characterize how the assessments were conducted, the exposure estimates, and the resulting MOEs.

6.3.1 Home Uses

6.3.2 Recreational Uses

6.3.3 Other (Spray Drift, etc.)

The following standard language has been developed by EXPO Sac for use in all HED risk assessment documents. As Agency policies are developed or modified, this language will be updated.

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for [chemical]. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. On a chemical by chemical basis, the Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic

methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift with specific products with significant risks associated with drift.

7.0 Aggregate Risk Assessments and Risk Characterization



RESOURCES:

HED SOP 97.2 Interim Guidance for Conducting Aggregate Exposure and Risk Assessments (11/26/97)
[See ▼SOPs ▼Aggregate]

“GUIDANCE FOR PERFORMING AGGREGATE EXPOSURE AND RISK ASSESSMENTS” (10/29/99)
[See ▲Science Policy Papers ➤Aggregate Exposure: Documents]

At the present time, the majority of HED risk assessments are conducted utilizing HED’s interim guidance provided in SOP97.2 and in the Document “ HED Risk Assessment Training” (Fall, 1998). In certain cases, it may be desirable to conduct a highly refined aggregate exposure assessment. Alternative methodologies utilizing models such as CARES and CALENDEX are available and have been utilized. See the Carbaryl and Atrazine IREDs for examples: <http://cfpub.epa.gov/oppre/rereg/status.cfm?show=rereg>.

Describe here, in a general sense, how the various exposure pathways have been addressed in conducting the aggregate exposure assessment. An example paragraph for this preamble follows:

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

Consider the following in the characterization of aggregate exposure and risk in the specific aggregate subsections below:

What types of data were used as inputs to the aggregate exposure estimate? Was each pathway of exposure estimated using a deterministic approach? Were all the inputs derived from deterministic assessments (e.g., point estimates of dietary exposure from DEEM and dermal exposure using Residential SOP screening-level assumptions)? Or does the aggregate exposure include inputs from both probabilistic and deterministic assessments? Did we combine highly refined dietary with unrefined residential assessment?

What are the uncertainties? Since all risks are not equal, qualitatively discuss the relative risk if MOEs appear to be a concern. Were screening level assessments used and what is their impact on the aggregate assessment? Have we added multiple screening level assessments together in our assessment, and if so, what is the implications for the reported aggregate risk? Which route of exposure or which application method results in the greatest risk to occupational users? To residential users? To children? To bystanders? In the diet? How strong are the data and how conservative are the assumptions that went into these estimates of risk?

There are several possible approaches for estimation of residues in drinking water: 1) comparison of a DWLOC to an EDWC; 2) incorporation of an EDWC directly into the dietary exposure assessment; and 3) a combination of DWLOC and EDWC calculations. One or both of the following paragraphs may be appropriate depending on the assessment.

For most pesticide active ingredients, water monitoring data are considered inadequate to determine surface and

ground water drinking water exposure estimates, so model estimates have been used to estimate residues in drinking water (EDWCs). In order to determine if aggregate risks are of concern, HED then calculates drinking water levels of comparison, or DWLOCs. The DWLOC is the maximum amount of a pesticide in drinking water that would be acceptable in light of combined exposure from food and residential pathways. The calculated DWLOCs are then compared to the EDWCs provided by EFED; if model-derived EDWCs exceed the DWLOCs for surface or ground water, there may be a concern for dietary exposure to residues in drinking water, and monitoring data may be required.

In order to fully implement the requirements of FQPA, HED and EFED have been working toward refining the screening-level DWLOC approach to conducting aggregate risk assessments that combine exposures across all pathways. As part of this process, EFED and HED have agreed that chronic and cancer EDWCs can be used directly in chronic/cancer dietary exposure assessments to calculate aggregate dietary (food + water) risk. This is done by using the relevant PRZM-EXAMS value as a residue for water (all sources) in the dietary exposure assessment. The principal advantage of this approach is that the actual individual body weight and water consumption data from the CSFII are used, rather than assumed weights and consumption for broad age groups. This refinement has been used for [chemical] chronic and cancer aggregate risk assessments for surface water, but not for the acute (surface and ground water) aggregate assessments.

Under each of the following sections, discuss the specifics of the pathways included in the aggregate assessment. Discuss the pathway-specific exposures, the DWLOCs, and the EDWCs as they relate to safety findings and levels of concern. Select and insert the appropriate aggregate table in the corresponding section.

7.1 Acute Aggregate Risk

7.2 Short-Term Aggregate Risk

7.3 Intermediate-Term Aggregate Risk

7.4 Long-Term Aggregate Risk

7.5 Cancer Risk

Table 6.x Aggregate Risk Assessment for Acute Dietary Exposure to [chemical].						
Population Subgroup ¹	Acute Scenario					
	aPAD mg/kg/day	Acute Food Exp mg/kg/day	Max Acute Water Exp mg/kg/day ₂	Ground Water EDWC (ppb) ³	Surface Water EDWC (ppb) ³	Acute DWLOC (ppb) ⁴
U.S. Population	0.0	0.0	0			0
All Infants (<1 year old)	0.0	0.0	0			0
Children 1-2 years old	0.0	0.0	0			0
Children 3-5 years old	0.0	0.0	0			0
Children 6-12 years old	0.0	0.0	0			0
Youth 13-19 years old	0.0	0.0	0			0
Adults 20-49 years old	0.0	0.0	0			0
Adults 50+ years old	0.0	0.0	0			0
Females 13-49 years old	0.0	0.0	0			0

¹ This footnote should indicate the selected subgroups and provide rationale for selection. Indicate body weights (70 kg adult male; 60 kg adult female; 10 kg child).

² Maximum acute water exposure (mg/kg/day) = [(aPAD (mg/kg/day) - acute food exposure (mg/kg/day))]

³ Provide model input assumptions e.g., crop, use parameters.

⁴ Acute DWLOC(μg/L) = $\frac{\text{maximum acute water exposure (mg/kg/day)} \times \text{body weight (kg)}}{[\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$

Table 7.x. Aggregate Risk Assessment for Chronic (Non-Cancer) Exposure to [Chemical]						
Population Subgroup¹	Chronic Scenario					
	cPAD mg/kg/day	Chronic Food Exp mg/kg/day	Max Chronic Water Exp mg/kg/day²	Ground Water EDWC (ppb)³	Surface Water EDWC (ppb)³	Chronic DWLOC (ppb)
U.S. Population	0.00	0.0	0			0
All Infants (<1 year old)	0.00	0.0	0			0
Children 1-2 years	0.00	0.0	0			0
Children 3-5 years	0.00	0.0	0			0
Children 6-12	0.00	0.0	0			0
Youth 13-19	0.00	0.0	0			0
Adults 20-49	0.00	0.0	0			0
Females 13+	0.00	0.0	0			0
Adults 50+ years	0.00	0.0	0			0

¹ This footnote should indicate the selected subgroups and provide rationale for selection. Indicate body weights (70 kg adult male; 60 kg adult female; 10 kg child).

²Maximum Chronic Water Exposure (mg/kg/day) = [Chronic PAD (mg/kg/day) - Chronic Dietary Exposure (mg/kg/day)]

³ Provide model input assumptions e.g., crop, use parameters.

⁴ Chronic DWLOC(μg/L) = $\frac{\text{maximum chronic water exposure (mg/kg/day)} \times \text{body weight (kg)}}{\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}}$

Table 7.x. Cancer DWLOC Calculations [Option 1: Risk is quantified using an MOE Approach]										
Population	Cancer Point of Departure mg/kg/day	Target MOE¹	Target Max Exposure² mg/kg/day	Chronic Food Exposure mg/kg/day	Residential Exposure (LADD) mg/kg/day	Aggregate MOE (food and residential)	Max Water Exposure³ mg/kg/day	Ground Water EDWC⁴ (ppb)	Surface Water⁴ EDWC (ppb)	Cancer DWLOC⁵ (µg/L)
Adult Male	0.00	100	0.000000	0.0000	0.000	0.00000	0.00000			0.00000
Adult Female										
Child										

¹ Indicate in this footnote the basis for the target MOE (include the standard inter- and intra- species safety factors totaling 100, as well as additional uncertainty factors/safety factors as appropriate.)

² Target Maximum Exposure (mg/kg/day) = POD (Point of Departure)/Target MOE

³ Maximum Water Exposure (mg/kg/day) = [Target Maximum Exposure - (Chronic Food Exposure + Residential Exposure (Lifetime Average Daily Dose))]

⁴ The crop producing the highest level was used.

⁵ Cancer DWLOC(µg/L) = $\frac{\text{maximum water exposure (mg/kg/day)} \times \text{body weight (kg)}}{\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}}$

Indicate body weights (70 kg adult male; 60 kg adult female; 10 kg child).

Table 7.x Cancer DWLOC Calculations [Option 2: Risk is quantified using an Q^* Approach]										
Population	Q^*	Negligible Risk Level ¹	Target Max Exposure ² mg/kg/day	Chronic Food Exposure mg/kg/day	Residential Exposure (LADD) mg/kg/day	Aggregate cancer risk (food and residential)	Max Water Exposure ³ mg/kg/day	Ground Water EDWC ⁴ (ppb)	Surface Water ⁴ EDWC (ppb)	Cancer DWLOC ⁵ (µg/L)
U.S. Pop	1.00e-06	0.000001	1.00000	0.000000	0.000000	0.00e+00	1.0000000			70000

¹ Indicate in this footnote the basis for the negligible risk if other than 1×10^{-6} .

² Target Maximum Exposure (mg/kg/day) = [negligible risk/ Q^*]

³ Maximum Water Exposure (mg/kg/day) = [Target Maximum Exposure - (Chronic Food Exposure + Residential Exposure (Lifetime Average Daily Dose))]

⁴ The crop producing the highest level was used.

⁵ Cancer DWLOC(µg/L) = $\frac{[\text{maximum water exposure (mg/kg/day)} \times \text{body weight (kg)}]}{[\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]^2}$

Table 7.x. Short-Term and/or Intermediate-Term Aggregate Risk and DWLOC Calculations (Option 1: Inhalation/Oral/Dermal Endpoints and NOAELs the Same)										
Population	Short or Intermediate-Term Scenario									
	NOAEL mg/kg/day	Target MOE ¹	Max Exposure ² mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure ³ mg/kg/day	Aggregate MOE (food and residential) ⁴	Max Water Exposure ⁵ mg/kg/day	Ground Water EDWC ⁶ (ppb)	Surface Water EDW C ⁶ (ppb)	Short-Term DWLOC ⁷ (µg/L)
Adult Male	0	100	0	0.000	0.000	??	0.000000			0
Adult Female	0	100	0	0.000	0.000	??	0.000000			0
Child	0	100	0	0.000	0.000	??	0.000000			0
Highest Exposed Adult Subpop ⁸										

¹ Indicate in this footnote the basis for the target MOE (include the standard inter- and intra- species safety factors totaling 100, as well as additional uncertainty factors/safety factors as appropriate.)

² Maximum Exposure (mg/kg/day) = NOAEL/Target MOE

³ Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure]

⁴ Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]

⁵ Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)

⁶ The crop producing the highest level was used.

⁷ DWLOC(µg/L) = $\frac{\text{maximum water exposure (mg/kg/day)} \times \text{body weight (kg)}}{[\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$ Indicate body weights and consumption

⁸Exposure refers to the highest **dietary** exposure.

Table 7.x. Short-Term and/or Intermediate-Term Aggregate Risk and DWLOC Calculations (Option 2: 1/MOE Approach - All Target MOEs Identical)											
Population	Short or Intermediate-Term Scenario										
	Target Aggregate MOE ¹	MOE food ²	MOE oral ³	MOE dermal ⁴	MOE inhalation ⁵	Aggregate MOE (food and residential) ⁶	MOE water ⁷	Allowable water exposure ⁸ (mg/kg/day)	Ground Water EDWC ⁹ (ppb)	Surface Water EDWC ⁹ (ppb)	DWLOC ¹⁰ (µg/L)
Adult Male											
Adult Female											
Child											
Highest Exposed Adult Subpop											

¹ Indicate in this footnote the basis for the target MOE.

² MOE food = [(short or intermediate-term oral NOAEL)/(chronic dietary exposure)] Indicate in footnote exposure and NOAEL used

³ MOE oral = [(short or intermediate-term oral NOAEL)/(hand-to-mouth residential exposure)] Indicate in footnote exposure and NOAEL used

⁴ MOE dermal = [(short or intermediate-term dermal NOAEL)/(high-end dermal residential exposure)] Indicate in footnote exposure and NOAEL used

⁵ MOE inhalation = [(inhalation NOAEL)/(high-end inhalation residential exposure)] Indicate in footnote exposure and NOAEL used

⁶ Aggregate MOE (food and residential) = $1 \div [(1 \div \text{MOE food}) + (1 \div \text{MOE oral}) + (1 \div \text{MOE dermal}) + (1 \div \text{MOE inhalation})]$

⁷ Water MOE = $1 \div [(1 \div \text{Target Aggregate MOE}) - (1 \div \text{Aggregate MOE (food and residential)})]$

⁸ Allowable water exposure = Short or Intermediate Term Oral NOAEL \div MOE water

⁹ The crop producing the highest level was used.

¹⁰ DWLOC(µg/L) = $\frac{\text{allowable water exposure (mg/kg/day)} \times \text{body weight (kg)}}{[\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$ Indicate body weights and consumption

Table 7.x. Short-Term and/or Intermediate-Term Aggregate Risk and DWLOC Calculations <i>(Option 3: 1/ARI Approach - All Target MOEs are not the same)</i>											
Population	Short or Intermediate-Term Scenario										
	ARI Food ¹	ARI oral ¹	ARI dermal ¹	ARI inhalation ¹	Aggregate ARI ²	ARI water ³	MOE water ⁴	Allowable water exposure ⁵ (mg/kg/day)	Ground Water EDWC ⁶ (ppb)	Surface Water EDWC ⁶ (ppb)	DWLOC ⁷ (µg/L)
Adult Male											
Adult Female											
Child											
Highest Exposed Adult Subpop											

¹ARI = [MOE_{CALCULATED} (i.e., FOOD, WATER, DERMAL, INHALATION, ORAL) ÷ MOE_{ACCEPTABLE}] (Note: Target ARI = 1)

$$^2\text{Aggregate ARI} = \frac{1}{\frac{1}{\text{ARI}_{\text{FOOD}}} + \frac{1}{\text{ARI}_{\text{WATER}}} + \frac{1}{\text{ARI}_{\text{ORAL}}} + \frac{1}{\text{ARI}_{\text{DERMAL}}} + \frac{1}{\text{ARI}_{\text{INHALATION}}}}$$

$$^3\text{ARI}_{\text{water}} = \frac{1}{\frac{1}{\text{ARI}_{\text{AGG}}} - \left[\frac{1}{\text{ARI}_{\text{FOOD}}} + \frac{1}{\text{ARI}_{\text{DERMAL}}} + \frac{1}{\text{ARI}_{\text{INHALATION}}} + \frac{1}{\text{ARI}_{\text{ORAL}}} \right]}$$

⁴MOE_{water} = ARI_{water} x Target MOE_{water}

⁵Allowable Water Exposure = NOAEL ÷ MOE_{water}

⁶The crop producing the highest level was used.

⁷DWLOC(µg/L) = $\frac{\text{allowable water exposure (mg/kg/day)} \times \text{body weight (kg)}}{[\text{water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$ Indicate body weights and consumption values used in footnote

8.0 Cumulative Risk Characterization/Assessment

The following standard language has been developed with OGC for use in all OPP risk assessment documents. As Agency policies are developed or modified, this language will be updated.

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to [chemical name] and any other substances and [chemical name] does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that [chemical name] has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

9.0 Occupational Exposure/Risk Pathway

Reference the Occupational/Residential Exposure Chapter/Memorandum here.

9.1 Short/Intermediate/Long-Term Handler Risk

Insert handler data and assumptions from the Occupational /Residential Exposure Chapter/Memorandum here. Characterize how the handler/applicator occupational exposure assessments were done, including major assumptions used to derive the exposure estimates.

Were there any scenarios for which data are lacking? Were any PHED scenario data extrapolated to other scenarios? Which routes of exposure contribute the most to total exposure? How do the uses and frequency of application relate to the duration of exposure? Which input parameters (unit exposure, application rate, acres treated, etc.) are central tendency vs. high-end values? What is the overall effect of these individual inputs on the outcome? What PPE are currently on existing/proposed labels? What PPE scenarios were included in the exposure and risk estimates?

Table 9.1. Short/Intermediate/Long-Term Occupational Exposure and Risk Estimates for [Chemical]. All estimates are at XXX mitigation (brief description of PPE). The dermal NOAEL is xxx mg/kg/day; the inhalation NOAEL is xxx mg/kg/day.					
Exposure Scenario (Scenario #)	Crop	Daily Dermal Dose, mg/kg/day	Daily Inhalation Dose, mg/kg/day	Dermal MOE	Inhalation MOE
Mixer/Loader					
	Crop 1				
	Crop 2				
	Crop 3				
Applicator					
	Crop 1				

Table 9.1. Short/Intermediate/Long-Term Occupational Exposure and Risk Estimates for [Chemical]. All estimates are at XXX mitigation (brief description of PPE). The dermal NOAEL is xxx mg/kg/day; the inhalation NOAEL is xxx mg/kg/day.					
Exposure Scenario (Scenario #)	Crop	Daily Dermal Dose, mg/kg/day	Daily Inhalation Dose, mg/kg/day	Dermal MOE	Inhalation MOE
	Crop 2				
	Crop 3				

9.2 Short/Intermediate/Long-Term Postapplication Risk

Insert postapplication data and assumptions from the Occupational/Residential Chapter/Memorandum here. Characterize how the postapplication occupational exposure assessments were done, including major assumptions used to derive the exposure estimates.

Were chemical-specific dislodgeable foliar residue (DFR) data or turf transferable residue (TTR) data available? Were the data crops tested translated to other crops? Does the assessment address metabolites or degradation products of toxicological concern in addition to the parent compound? Do dissipation patterns (modeled or empirically derived) concur with dissipation information from environmental fate data?

Table 9.2. Postapplication Occupational Exposure and Risk Estimates for Chemical. All estimates are for zero days after the final application.			
Crop	Work Activity	Daily Dose (mg/kg/day)	MOE
Crop 1	Activity 1		
	Activity 2		
Crop 2	Activity 1		
	Activity 2		
Crop 3	Activity 1		
	Activity 2		

10.0 Data Needs and Label Requirements

For each guideline series, what data remain outstanding - provide a detailed listing by guideline since this is often the section the risk managers turns to as a definitive list of data requirements. Are confirmatory or condition of registration data required? Are any revisions required to the label - clearly list all necessary label amendments.

10.1 Toxicology

10.2 Residue Chemistry

10.3 Occupational and Residential Exposure

References:

[Reference all supporting documents (HIARC Report, MARC Report, Chemistry Chapter, ORE Chapter, etc.)]

Appendices

1.0 TOXICOLOGY DATA REQUIREMENTS

Table 1. Insert yes, no, or “-” as appropriate. Use foot notes to indicate where the guideline is satisfied by studies of a different guideline requirement, or when there is something unusual (e.g. Waiver, a formulation is used to satisfy the technical requirement.)

The requirements (40 CFR 158.340) for [[Type of Use \(e.g., food vs. non food\)](#)] for [[CHEMICAL NAME](#)] are in Table 1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Test	Technical	
	Required	Satisfied
870.1100 Acute Oral Toxicity	yes	yes
870.1200 Acute Dermal Toxicity	yes	yes
870.1300 Acute Inhalation Toxicity	yes	yes
870.2400 Primary Eye Irritation	yes	yes
870.2500 Primary Dermal Irritation	yes	yes
870.2600 Dermal Sensitization	yes	yes
870.3100 Oral Subchronic (rodent)		
870.3150 Oral Subchronic (nonrodent)		
870.3200 21-Day Dermal		
870.3250 90-Day Dermal		
870.3465 90-Day Inhalation		
870.3700a Developmental Toxicity (rodent)		
870.3700b Developmental Toxicity (nonrodent)		
870.3800 Reproduction		
870.4100a Chronic Toxicity (rodent)		
870.4100b Chronic Toxicity (nonrodent)		
870.4200a Oncogenicity (rat)		
870.4200b Oncogenicity (mouse)		
870.4300 Chronic/Oncogenicity		
870.5100 Mutagenicity—Gene Mutation - bacterial		
870.5300 Mutagenicity—Gene Mutation - mammalian		
870.5xxx Mutagenicity—Structural Chromosomal Aberrations ..		
870.5xxx Mutagenicity—Other Genotoxic Effects		
870.6100a Acute Delayed Neurotox. (hen)	no	-
870.6100b 90-Day Neurotoxicity (hen)	no	-
870.6200a Acute Neurotox. Screening Battery (rat)		
870.6200b 90 Day Neuro. Screening Battery (rat)		
870.6300 Develop. Neuro		

Test	Technical	
	Required	Satisfied
870.7485 General Metabolism		
870.7600 Dermal Penetration		
Special Studies for Ocular Effects		
Acute Oral (rat)		
Subchronic Oral (rat)		
Six-month Oral (dog)		

2.0 NON-CRITICAL TOXICOLOGY STUDIES

Executive Summaries for studies not used for toxicity endpoint selection or FQPA assessment are included here.

3.0 METABOLISM CONSIDERATIONS

1.07_Introduction

07.1_Description of Issues

07.2_Team Proposal

2.0 Nature of the Residue Studies in Plants

2.1.1 Executive Summary of Plant Study No. 1

Executive summary may be edited to remove information not critical to HEXARC decision making

2.1.2 Tabular Summary of Plant Study No. 1

Table C.2.3 from Nature of the Residue DER Template

2.1.3 Executive Summary of Plant Study No. 2

Executive summary may be edited to remove information not critical to HEXARC decision making

2.1.4 Tabular Summary of Plant Study No. 2

Table C.2.3 from Nature of the Residue DER Template

..... to

2.1.(n+2) Executive Summary of Plant Study No. n

Executive summary may be edited to remove information not critical to HEXARC decision making

2.1.(2n) Tabular Summary of Plant Study No. n

Table C.2.3 from Nature of the Residue DER Template

3.0 Nature of the Residue in Livestock

3.1.1 Executive Summary of Ruminant Study

Executive summary may be edited to remove information not critical to HEXARC decision making

3.1.2 Tabular Summary of Ruminant Study

Table C.2.3 from Nature of the Residue DER Template

3.1.3 Executive Summary of Poultry Study

Executive summary may be edited to remove information not critical to HEXARC decision making

3.1.4 Tabular Summary of Poultry Study

Table C.2.3 from Nature of the Residue DER Template

3.1.5 Executive Summary of Swine Study (or any other livestock metabolism study)

Executive summary may be edited to remove information not critical to HEXARC decision making

3.1.6 Tabular Summary of Swine Study (or any other livestock metabolism study)

Table C.2.3 from Nature of the Residue DER Template

4.0 Confined Rotational Crop Studies

4.1 Executive Summary of Rotational Crop Study

Executive summary may be edited to remove information not critical to HEXARC decision making

4.2 Tabular Summary of Rotational Crop Study

Table (get number) from Residue Chemistry DER Template

5.0 Analytical Methodology
Complete the following table:

Method Name	Applicable Commodities	Analytes	Extraction Solvent(s)	Clean-up Step(s)	Determinative Step	LOQ, ppm	LOD, ppm

6.0 Summary of Magnitude of Residue (MOR) Studies

6.1 Plants

Briefly summarize the MOR studies in one table. Note the table should have summaries on a commodity basis, not trial basis. Results should be ranges; individual values are not needed. Include level of exaggeration in Tables. See example tables on following pages.

6.2 Livestock

Briefly summarize the MOR (feeding) studies in one table. Note the table should have summaries on a commodity basis, not trial basis. Results should be ranges; individual values are not needed. Include Dietary burden in description and level of exaggeration in Tables. See example tables on following pages.

6.3 Rotational Crops (Optional)

Briefly summarize the limited and extensive rotational crop field trials.

7.0 International Considerations

Information on the tolerance definitions for Codex and any other international bodies.

8.0 Environmental Degradation

8.1 Environmental Persistence

8.2 Expected Mobility

8.3 Environmental Metabolites

8.3.1 Parent and Degradates in Laboratory and Field Studies

8.3.2 Environmental Degradates

Summary of Magnitude of Residue Studies for _____

Note: May also use table from Residue Chemistry Summary Document Template, Section on 860.1500

[illegible]

Summary of Livestock Feeding Studies For _____

Commodity	Feeding ¹ Level,	Parent		Metabolite 1		Metabolite 2		Metabolite 3	
		Range of Residues, ppm	Average, ppm	Range of Residues, ppm	Average , ppm	Range of Residues, ppm	Average, ppm	Range of Residues, ppm	Average, ppm
Milk	L ppm								
	M								
	H								
Ruminant Muscle	L								
	M								
	H								
Ruminant Fat	L								
	M								
	H								
Ruminant Liver	L								
	M								
	H								
Ruminant Kidney	L								
	M								
	H								
Eggs	L								
	M								
	H								
Poultry Muscle	L								
	M								
	H								
Poultry Fat	L								
	M								
	H								
Poultry Liver	L								
	M								
	H								
	L								

Commodity	Feeding ¹ Level,	Parent		Metabolite 1		Metabolite 2		Metabolite 3	
		Range of Residues, ppm	Average, ppm	Range of Residues, ppm	Average , ppm	Range of Residues, ppm	Average, ppm	Range of Residues, ppm	Average, ppm
Poultry Kidney	M ppm								
	H								

¹ Feeding level L = 1x level, M = 4x, H = 11x for ruminants; do the same for poultry

Degradate Name ¹	Report % Applied Dose, PPM, T _{1/2} , Other Pertinent Information ²							Monitoring Data Available? ⁴	Cleaned Up By Drinking Water Treatment? ⁵
	Aerobic Soil Metabolism	Anaerobic Soil Metabolism	Field Dissipation	Aerobic Aquatic Metabolism	Anaerobic Aquatic Metabolism	Photolysis	Hydrolysis		
Parent									
Degradate 1									
Degradate 2									
Degradate 3									
Study MRID No.									
Study Characterization ³									

¹ All degradates should be listed, not just the top three.

² Include information that would be critical for supporting the risk assessment team proposal. In all cases the %of applied dose and/or ppm (in the field dissipation studies should be included.

³ Is the study a good study? Core? Supplemental? Inadequate? Non-existent?

⁴ If yes, briefly describe the monitoring data in the drinking water characterization section.

⁵ If yes, cite the basis on drinking water treatment in the drinking water characterization section.

Additional Information to Assist Risk Assessment Teams:

Considerations for Environmental Degradation Section (3.3)

This should be descriptive and contain language that describes the degradates that are likely to be found in drinking water. It should NOT be a detailed fate description, but should include information to support the team proposal and describe the uncertainties in that proposal. Below are lists of considerations that should be included; note that all of them will not apply to every situation. HED is relying upon the judgement and expertise of EFED scientists to use these considerations that often arise during discussions to characterize the potential for a pesticide and/or its degradates to reach human drinking water.

Considerations and Examples:

- What is the primary route of dissipation in the environment? (e.g. microbial metabolism in soil, runoff, aquatic photolysis in rice water, etc.)
- What are the most important routes by which the pesticide and its degradates get into drinking water? (e.g. surface water runoff, leaching to groundwater, etc.)
- What data are available to support the hypothesis on how the pesticide and degradates will get into drinking water?
- How do the use patterns and application methods support your argument? (e.g. pesticide is soil incorporated, so little is expected to be available for soil photolysis)
- What are the significant uncertainties in your assessment?
- Are data available on the persistence and mobility of the degradates?
- Do you expect the concentration of the degradates to exceed the concentration of the parent, considering peak and chronic exposures? (e.g. are degradates more mobile and/or persistent than parent?)
- Does Office of Water have any MCLs or is otherwise involved with the pesticide and/or its degradates? (Some degradates may have other non-pesticidal uses, e.g. ETU.)
- If degradates are likely to occur in drinking water sources, using your judgement, at what order of magnitude will they be found? (e.g. PPM, PPB, PPT)

- Are monitoring data available for degradates? What do the monitoring data show?
- Did the registrant look for the degradates in the field dissipation study? If so, were they detected?
- Are there any prospective or retrospective ground water studies?
- Are there data showing the fate of the pesticide and its degradates in water treatment systems? If not, do you have an opinion on what could happen? (e.g. pesticide is very non-polar, so would likely be removed during flocculation)

Considerations for Toxicity Profile of Major Metabolites and Degradates (3.5)

If there is going to be significant exposure to pesticide metabolites and environmental degradates, then the risk assessment team should do some investigation into the potential toxicity of the metabolites and degradates. This background information will be used to support the teams rationale for including the metabolites and degradates in the risk assessment. In some rare cases, the office may have received toxicity data on the metabolites. In the absence of data on the metabolites, at a minimum the team should do the following: 1) literature search on major metabolites; 2) consult with SAR experts; 3) determine if the significant metabolites are common metabolites with other pesticides. When reporting results of the literature search in the briefing document, the team should describe what sources were consulted. Alberto Protzel has performed this function for the MARC in the past and can advise the team on the best resources. The team is advised to consult with Leonard Kiefer (OPPT) and/or Alberto Protzel (OPP) for information on structure activity relationships. If they are not able to provide assistance they have access to resources that may be helpful. A single resource is not readily available for determining common metabolites with other chemicals. However, when scoping the chemical for the initial RARC meeting, the team will likely determine its chemical class. The team is advised to review assessments for other chemicals in the class for common metabolites. In fact data on common metabolites may have been submitted in association with other registrations. Such information should be included.

This section of the document should be descriptive. As the type of information can vary widely, no prescribed format should be followed. In

most cases this section will be brief; if information is available, then a summary should be provided here and details should only be provided if it is relevant for the decision. For example if a similar metabolite has been regulated for other chemicals in a class, then a brief summary should be sufficient. If however, the team decides that regulation of the subject chemical should be different than others in its class, then the team needs to provide sufficient hazard information that would guide members of the HEXARC towards that decision as well